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NEWS	3	OCT 04	Precision of EMBASE searching enhanced with new chemical name field
NEWS	4	OCT 06	Increase your retrieval consistency with new formats or for Taiwanese application numbers in CA/CAPLUS.
NEWS	5	OCT 21	CA/CAPLUS kind code changes for Chinese patents increase consistency, save time
NEWS	6	OCT 22	New version of STN Viewer preserves custom highlighting of terms when patent documents are saved in .rtf format
NEWS	7	OCT 28	INPADOCDB/INPAFAMDB: Enhancements to the US national patent classification.
NEWS	8	NOV 03	New format for Korean patent application numbers in CA/CAPLUS increases consistency, saves time.
NEWS	9	NOV 04	Selected STN databases scheduled for removal on December 31, 2010
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\*\*\*\*\* STN Columbus \*\*\*\*\*

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COST IN U.S. DOLLARS

SINCE FILE

TOTAL

ENTRY

SESSION

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0.46

0.46

FILE 'REGISTRY' ENTERED AT 10:07:50 ON 05 JAN 2011

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=> e arimoclomol

E1	1	ARIMIDS/BI
E2	1	ARIMOCLOM/BI
E3	1 -->	ARIMOCLOMOL/BI
E4	2	ARIMOL/BI
E5	2	ARIMOSA/BI
E6	1	ARIMOTO/BI
E7	158	ARIN/BI
E8	19	ARINA/BI
E9	18	ARINAE/BI
E10	1	ARINAMINE/BI
E11	4	ARINATE/BI
E12	56	ARINE/BI

=> s e3

L1 1 ARIMOCLOMOL/BI

=> file caplus medline biosis embase

COST IN U.S. DOLLARS

SINCE FILE

TOTAL

ENTRY

SESSION

FULL ESTIMATED COST

6.21

6.67

FILE 'CAPLUS' ENTERED AT 10:08:14 ON 05 JAN 2011

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FILE 'EMBASE' ENTERED AT 10:08:14 ON 05 JAN 2011

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=> s (l1 or arimoclomol)

L2 112 (L1 OR ARIMOCLOMOL)

=> dup rem l2

PROCESSING COMPLETED FOR L2

L3 88 DUP REM L2 (24 DUPLICATES REMOVED)

=> s l3 and (als or amyotrophic)

L4 28 L3 AND (ALS OR AMYTROPHIC)

=> d l4 ibib abs

L4 ANSWER 1 OF 28 CAPLUS COPYRIGHT 2011 ACS on STN

ACCESSION NUMBER: 2010:919711 CAPLUS

TITLE: Arimoclomol, a coinducer of heat shock proteins for the potential treatment of amyotrophic lateral sclerosis

AUTHOR(S): Phukan, Julie

CORPORATE SOURCE: Department of Neurology, Royal Free Hospital, London, NW3 2QG, UK

SOURCE: IDrugs (2010), 13(7), 482-496

CODEN: IDRUFN; ISSN: 2040-3410

URL: <http://www.biomedcentral.com/content/pdf/cd-1110350.pdf>

BioMed Central Ltd.

PUBLISHER: Journal; General Review; (online computer file)

DOCUMENT TYPE: English

AB Recent years have seen an explosion of research into increasingly prevalent neurodegenerative diseases. Arimoclomol (BRX-220), being developed by CytRx Corp, is an oral therapeutic candidate for the treatment of amyotrophic lateral sclerosis (ALS), the most common form of motor neuron disease. ALS is a fatal, incurable disorder, which can present as sporadic (90 to 95% of cases) or familial (5 to 10% of cases) forms. The etiol. of sporadic ALS remains unknown and much of the understanding of ALS pathogenesis has been derived through study of its familial forms; in particular, through study of autosomal dominant mutations in the SOD1 (copper/zinc superoxide dismutase) gene, which cause approx. 20% of familial ALS cases. Under conditions of excessive stress, arimoclomol induces amplification of the cytoprotective heat shock response in order to protect motor neurons from death. Comprehensive in vivo and in vitro studies demonstrated its effect in the prevention of neuronal loss and promotion of motor neuron survival, even after symptom onset. Clin. trials have reported good tolerability and safety. This paper discusses the rationale for arimoclomol use in ALS, the preclin. and clin. evidence collected to date, the likelihood of its promising preclin. results translating to humans, and the relevance of this research for neurodegeneration as a whole.

REFERENCE COUNT: 126 THERE ARE 126 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

=> d 14 ibib abs 2-28

L4 ANSWER 2 OF 28 CAPLUS COPYRIGHT 2011 ACS on STN

ACCESSION NUMBER: 2009:1472488 CAPLUS

DOCUMENT NUMBER: 152:110625

TITLE: Arimoclomol: a potential therapy under development for ALS

AUTHOR(S): Lanka, Veena; Wieland, Scott; Barber, Jack; Cudkowicz, Merit

CORPORATE SOURCE: Neurology Clinical Trial Unit, Charlestown, MA, 02129, USA

SOURCE: Expert Opinion on Investigational Drugs (2009), 18(12), 1907-1918

CODEN: EOIDER; ISSN: 1354-3784

PUBLISHER: Informa Healthcare

DOCUMENT TYPE: Journal; General Review

LANGUAGE: English

AB A review. Arimoclomol, an amplifier of heat shock protein expression involved in cellular stress response, has emerged as a potential therapeutic candidate in amyotrophic lateral sclerosis (ALS) in recent years. Treatment with arimoclomol was reported to improve survival and muscle function in a mouse model of motor neuron disease. Several single- and multiple-dose safety studies have been completed in healthy control subjects. A 3-mo Phase IIA study in people with ALS demonstrated safety at dosages up to 300 mg/day and another study is currently recruiting participants with familial ALS caused by mutations in the superoxide dismutase gene. We review the rationale for testing arimoclomol in sporadic and familial ALS in the context of available safety and pharmacokinetic data. Published and unpublished literature relative to the drug in the past two decades is discussed. The current review attempts to bring together our existing understanding of the actions of arimoclomol with the disease profile of ALS. The pharmacol. profile of arimoclomol and the available preclin. data make it a promising therapeutic possibility in ALS.

OS.CITING REF COUNT: 6 THERE ARE 6 CAPLUS RECORDS THAT CITE THIS RECORD (6 CITINGS)

REFERENCE COUNT: 86 THERE ARE 86 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 3 OF 28 CAPLUS COPYRIGHT 2011 ACS on STN

ACCESSION NUMBER: 2008:1320737 CAPLUS

DOCUMENT NUMBER: 149:548757

TITLE: Late stage treatment with arimoclomol delays disease progression and prevents protein aggregation in the SOD1G93A mouse model of ALS

AUTHOR(S): Kalmar, Bernadett; Novoselov, Sergey; Gray, Anna; Cheetham, Michael E.; Margulis, Boris; Greensmith, Linda

CORPORATE SOURCE: Institute of Neurology, University College London, London, UK

SOURCE: Journal of Neurochemistry (2008), 107(2), 339-350

CODEN: JONRA9; ISSN: 0022-3042

PUBLISHER: Wiley-Blackwell

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Amyotrophic lateral sclerosis (ALS) is a progressive neurodegenerative disorder characterized by motoneuron degeneration, resulting in muscle paralysis and death, typically within 1-5 years of diagnosis. Although the pathogenesis of ALS remains unclear, there is evidence for the involvement of proteasome dysfunction and heat shock proteins in the disease. We have previously shown that treatment

with a co-inducer of the heat shock response called arimoclomol is effective in the SODG93A mouse model of ALS, delaying disease progression and extending the lifespan of SODG93A mice. However, this previous study only examined the effects arimoclomol when treatment was initiated in pre- or early symptomatic stages of the disease. Clearly, to be of benefit to the majority of ALS patients, any therapy must be effective after symptom onset. In order to establish whether post-symptomatic treatment with arimoclomol is effective, in this study we carried out a systematic assessment of different treatment regimes in SODG93A mice. Treatment with arimoclomol from early (75 days) or late (90 days) symptomatic stages significantly improved muscle function. Treatment from 75 days also significantly increased the lifespan of SODG93A mice, although treatment from 90 days has no significant effect on lifespan. The mechanism of action of arimoclomol involves potentiation of the heat shock response, and treatment with arimoclomol increased Hsp70 expression. Interestingly, this up-regulation in Hsp70 was accompanied by a decrease in the number of ubiquitin-pos. aggregates in the spinal cord of treated SODG93A mice, suggesting that arimoclomol directly effects protein aggregation and degradation

OS.CITING REF COUNT: 18 THERE ARE 18 CAPLUS RECORDS THAT CITE THIS RECORD (18 CITINGS)  
 REFERENCE COUNT: 34 THERE ARE 34 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 4 OF 28 CAPLUS COPYRIGHT 2011 ACS ON STN

ACCESSION NUMBER: 2008:918262 CAPLUS

DOCUMENT NUMBER: 149:258394

TITLE: Arimoclomol at dosages up to 300 Mg/day is well tolerated and safe in amyotrophic lateral sclerosis

AUTHOR(S): Cudkowicz, Merit E.; Shefner, Jeremy M.; Simpson, Elizabeth; Grasso, Daniela; Yu, Hong; Zhang, Hui; Shui, Amy; Schoenfeld, David; Brown, Robert H.; Wieland, Scott; Barber, Jack R.

CORPORATE SOURCE: NORTHEAST ALS CONSORTIUM, Neurology Clinical Trials Unit, Massachusetts General Hospital, Charlestown, MA, 02129, USA

SOURCE: Muscle & Nerve (2008), 38(1), 837-844

CODEN: MUNEDE; ISSN: 0148-639X

PUBLISHER: John Wiley & Sons, Inc.

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Arimoclomol is an investigational drug for amyotrophic lateral sclerosis (ALS) that amplifies heat shock protein gene expression during cell stress. The objectives of the present study were to assess the safety, tolerability, and pharmacokinetics of arimoclomol in ALS. Eighty-four participants with ALS received arimoclomol at one of three oral doses (25, 50, or 100 mg three times daily) or placebo. The primary outcome measure was safety and tolerability. A subset of 44 participants provided serum and cerebrospinal fluid (CSF) samples for pharmacokinetic anal. Participants who completed 12 wk of treatment could enroll in a 6-mo open-label study. Arimoclomol at doses up to 300 mg/day was well tolerated and safe. Arimoclomol resulted in dose-linear pharmacol. exposures and the half-life did not change with continued treatment. Arimoclomol CSF levels increased with dose. Arimoclomol was shown to be safe, and it crosses the blood-brain barrier. Serum pharmacokinetic profiles support dosing of three times per day. An efficacy study in ALS is planned.

OS.CITING REF COUNT: 15 THERE ARE 15 CAPLUS RECORDS THAT CITE THIS RECORD (15 CITINGS)

REFERENCE COUNT: 27 THERE ARE 27 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 5 OF 28 CAPLUS COPYRIGHT 2011 ACS ON STN

ACCESSION NUMBER: 2007:1424894 CAPLUS

DOCUMENT NUMBER: 148:492092

TITLE: Heat shock proteins and protection of the nervous system

AUTHOR(S): Brown, Ian R.

CORPORATE SOURCE: Center for the Neurobiology of Stress, University of Toronto at Scarborough, Toronto, ON, Can.

SOURCE: Annals of the New York Academy of Sciences (2007), 1113(Stress Responses in Biology and Medicine), 147-158

CODEN: ANYAA9; ISSN: 0077-8923

PUBLISHER: Blackwell Publishing, Inc.

DOCUMENT TYPE: Journal; General Review

LANGUAGE: English

AB A review. Manipulation of the cellular stress response offers strategies to protect brain cells from damage induced by ischemia and neurodegenerative diseases. Overexpression of Hsp70 reduced ischemic injury in the mammalian brain. Investigation of the domains within Hsp70 that confers ischemic neuroprotection revealed the importance of the carboxyl-terminal domain. Arimoclomol, a coinducer of heat shock proteins, delayed progression of amyotrophic lateral sclerosis (ALS) in a mouse model in which motor neurons in the spinal cord and motor cortex degenerate. Celastrol, a promising candidate as an agent to counter neurodegenerative diseases, induced expression of a set of Hsps in differentiated neurons grown in tissue culture. Heat shock "preconditioning" protected the nervous system at the functional level of the synapse and selective overexpression of Hsp70 enhanced the level of synaptic protection. Following hyperthermia, constitutively expressed Hsc70 increased in synapse-rich areas of the brain where it associates with Hsp40 to form a complex that can refold denatured proteins. Stress tolerance in neurons is not solely dependent on their own Hsps but can be supplemented by Hsps from adjacent glial cells. Hence, application of exogenous Hsps at neural injury sites is an effective strategy to maintain neuronal viability.

OS.CITING REF COUNT: 37 THERE ARE 37 CAPLUS RECORDS THAT CITE THIS RECORD (38 CITINGS)

REFERENCE COUNT: 72 THERE ARE 72 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 6 OF 28 CAPLUS COPYRIGHT 2011 ACS ON STN

ACCESSION NUMBER: 2007:711978 CAPLUS

DOCUMENT NUMBER: 147:377138

TITLE: Emerging disease-modifying therapies for the treatment of motor neuron disease/amyotrophic lateral sclerosis

AUTHOR(S): Bedlack, Richard S.; Traynor, Bryan J.; Cudkowicz, Merit E.

CORPORATE SOURCE: Duke University Medical Center, Durham, NC, USA

SOURCE: Expert Opinion on Emerging Drugs (2007), 12(2), 229-252

CODEN: EOEDA3

PUBLISHER: Informa Healthcare

DOCUMENT TYPE: Journal; General Review

LANGUAGE: English

AB A review. It has been > 130 years since the first description of the upper and lower motor neuron disease called amyotrophic lateral sclerosis (ALS). Sadly, there has been little change in the long interval over which this disease is diagnosed, or in its poor prognosis. Significant gains have been made, however, in understanding its

pathophysiol. and in symptomatic care. Disease-causing mutations have been identified and used to create animal models. Other identified mutations may increase susceptibility and cause disease only in a particular environment and at a particular age. A number of 'downstream' mol. pathways have been implicated, including transcriptional disturbances, protein aggregation, excitotoxicity, mitochondrial dysfunction, oxidative stress, neuroinflammation, cytoskeletal and axonal transport derangements, growth factor dysregulation and apoptosis. This knowledge has led to an impressive pipeline of candidate therapies that offer hope for finally being able to alter ALS disease progression. These are described and prioritized herein, and suggestions are offered for efficiently sifting through them.

OS.CITING REF COUNT: 5 THERE ARE 5 CAPLUS RECORDS THAT CITE THIS RECORD  
(5 CITINGS)  
REFERENCE COUNT: 148 THERE ARE 148 CITED REFERENCES AVAILABLE FOR  
THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE  
FORMAT

L4 ANSWER 7 OF 28 CAPLUS COPYRIGHT 2011 ACS ON STN

ACCESSION NUMBER: 2006:598700 CAPLUS

DOCUMENT NUMBER: 145:499471

TITLE: Neuroprotective agents for clinical trials in  
ALS

AUTHOR(S): Traynor, B. J.; Bruijn, L.; Conwit, R.; Beal, F.;  
O'Neill, G.; Fagan, S. C.; Cudkovicz, M. E.

CORPORATE SOURCE: Neurology Clinical Trials Unit, Department of  
Neurology, Massachusetts General Hospital, Boston, MA,  
USA

SOURCE: Neurology (2006), 67(1), 20-27  
CODEN: NEURAI; ISSN: 0028-3878

PUBLISHER: Lippincott Williams & Wilkins

DOCUMENT TYPE: Journal; General Review

LANGUAGE: English

AB A review. Background: Riluzole is currently the only Food and Drug Administration-approved treatment for ALS, but its effect on survival is modest. Objective: To identify potential neuroprotective agents for testing in phase III clin. trials and to outline which data need to be collected for each drug. Methods: The authors identified 113 compds. by inviting input from academic clinicians and researchers and via literature review to identify agents that have been tested in ALS animal models and in patients with ALS. The list was initially narrowed to 24 agents based on an evaluation of scientific rationale, toxicity, and efficacy in previous animal and human studies. These 24 drugs underwent more detailed pharmacol. evaluation. Results: Twenty drugs were selected as suitable for further development as treatments for patients with ALS. Talampanel and tamoxifen have completed early phase II trials and have demonstrated preliminary efficacy. Other agents (ceftriaxone, minocycline, ONO-2506, and IGF-1 polypeptide) are already in phase III trials involving large nos. of patients with ALS. Remaining agents (AEOL 10150, arimoclomol, celastrol, coenzyme Q10, copaxone, IGF-1-viral delivery, memantine, NAALADase inhibitors, nimesulide, scriptaid, sodium phenylbutyrate, thalidomide, trehalose) require addnl. preclin. animal data, human toxicity and pharmacokinetic data including CNS penetration prior to proceeding to large scale phase III human testing. Further development of riluzole analogs should be considered. Conclusions: Several potential neuroprotective compds., representing a wide range of mechanisms, are available and merit further investigation in ALS.

OS.CITING REF COUNT: 48 THERE ARE 48 CAPLUS RECORDS THAT CITE THIS  
RECORD (48 CITINGS)  
REFERENCE COUNT: 86 THERE ARE 86 CITED REFERENCES AVAILABLE FOR THIS  
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 8 OF 28 CAPLUS COPYRIGHT 2011 ACS on STN  
 ACCESSION NUMBER: 2004:263763 CAPLUS  
 DOCUMENT NUMBER: 140:399884  
 TITLE: Treatment with arimoclomol, a coinducer of heat shock proteins, delays disease progression in ALS mice  
 AUTHOR(S): Kieran, Dairin; Kalmar, Bernadett; Dick, James R. T.; Riddoch-Contreras, Joanna; Burnstock, Geoffrey; Greensmith, Linda  
 CORPORATE SOURCE: The National Hospital for Neurology and Neurosurgery, Institute of Neurology, Sobell Department of Motor Neuroscience and Movement Disorders, The Graham Watts Laboratory, University College London, London, WC1N 3BG, UK  
 SOURCE: Nature Medicine (New York, NY, United States) (2004), 10(4), 402-405  
 CODEN: NAMEFI; ISSN: 1078-8956  
 PUBLISHER: Nature Publishing Group  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English  
 AB Amyotrophic lateral sclerosis (ALS) is a fatal neurodegenerative condition in which motoneurons of the spinal cord and motor cortex die, resulting in progressive paralysis. This condition has no cure and results in eventual death, usually within 1-5 yr of diagnosis. Although the specific etiol. of ALS is unknown, 20% of familial cases of the disease carry mutations in the gene encoding Cu/Zn superoxide dismutase-1 (SOD1). Transgenic mice overexpressing human mutant SOD1 have a phenotype and pathol. that are very similar to that seen in human ALS patients. Here we show that treatment with arimoclomol, a coinducer of heat shock proteins (HSPs), significantly delays disease progression in mice expressing a SOD1 mutant in which glycine is substituted with alanine at position 93 (SOD1G93A). Arimoclomol-treated SOD1G93A mice show marked improvement in hind limb muscle function and motoneuron survival in the later stages of the disease, resulting in a 22% increase in lifespan. Pharmacol. activation of the heat shock response may therefore be a successful therapeutic approach to treating ALS, and possibly other neurodegenerative diseases.  
 OS.CITING REF COUNT: 174 THERE ARE 174 CAPLUS RECORDS THAT CITE THIS RECORD (174 CITINGS)  
 REFERENCE COUNT: 20 THERE ARE 20 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 9 OF 28 MEDLINE on STN  
 ACCESSION NUMBER: 2004163909 MEDLINE  
 DOCUMENT NUMBER: PubMed ID: 15057226  
 TITLE: Putting the heat on ALS.  
 AUTHOR: Benn Susanna C; Brown Robert H Jr  
 SOURCE: Nature medicine, (2004 Apr) Vol. 10, No. 4, pp. 345-7.  
 Journal code: 9502015. ISSN: 1078-8956. L-ISSN: 1078-8956.  
 PUB. COUNTRY: United States  
 DOCUMENT TYPE: Commentary  
 NEWS ANNOUNCEMENT  
 LANGUAGE: English  
 FILE SEGMENT: Priority Journals  
 ENTRY MONTH: 200406  
 ENTRY DATE: Entered STN: 2 Apr 2004  
 Last Updated on STN: 9 Jun 2004  
 Entered Medline: 8 Jun 2004

L4 ANSWER 10 OF 28 BIOSIS COPYRIGHT (c) 2011 The Thomson Corporation on



STN  
 ACCESSION NUMBER: 2008:65583 BIOSIS  
 DOCUMENT NUMBER: PREV200800069044  
 TITLE: Heat shock proteins and protection of the nervous system.  
 AUTHOR(S): Brown, Ian R. [Reprint Author]  
 CORPORATE SOURCE: Univ Toronto Scarborough, Ctr Neurobiol Stress, 1265 Mil  
 Trail, Toronto, ON M1C 1A4, Canada  
 ibrown@utsc.utoronto.ca  
 SOURCE: Csernely, P [Editor]; Korcsmaros, T [Editor]; Sulyok, K  
 [Editor]. Ann. N. Y. Acad. Sci., (2007) pp. 147-158. Annals  
 of the New York Academy of Sciences: STRESS OF LIFE IN  
 MOLECULES, CELLS, ORGANISMS, AND PSYCHOSOCIAL COMMUNITIES.  
 Publisher: BLACKWELL PUBLISHING, 9600 GARSINGTON RD, OXFORD  
 OX4 2DQ, OXEN, UK. Series: ANNALS OF THE NEW YORK ACADEMY  
 OF SCIENCES.  
 Meeting Info.: 2nd World Conference on Stress. Budapest,  
 HUNGARY. August 23 -26, 2007.  
 CODEN: ANYAA9. ISSN: 0077-8923. ISBN: 978-1-57331-675-0(S).  
 DOCUMENT TYPE: Book; (Book Chapter)  
 Conference; (Meeting)  
 LANGUAGE: English  
 ENTRY DATE: Entered STN: 9 Jan 2008  
 Last Updated on STN: 31 Dec 2008  
 AB Manipulation of the cellular stress response offers strategies to protect  
 brain cells from damage induced by ischemia and neurodegenerative  
 diseases. Overexpression of Hsp70 reduced ischemic injury in the  
 mammalian brain. Investigation of the domains within Hsp70 that confers  
 ischemic neuroprotection revealed the importance of the carboxyl-terminal  
 domain. Arimoclomol, a coinducer of heat shock proteins,  
 delayed progression of amyotrophic lateral sclerosis (ALS) in a  
 mouse model in which motor neurons in the spinal cord and motor cortex  
 degenerate. Celastrol, a promising candidate as an agent to counter  
 neurodegenerative diseases, induced expression of a set of Hsps in  
 differentiated neurons grown in tissue culture. Heat shock  
 "preconditioning" protected the nervous system at the functional level of  
 the synapse and selective overexpression of Hsp70 enhanced the level of  
 synaptic protection. Following hyperthermia, constitutively expressed  
 Hsc70 increased in synapse-rich areas of the brain where it associates  
 with Hsp40 to form a complex that can refold denatured proteins. Stress  
 tolerance in neurons is not solely dependent on their own Hsps but can be  
 supplemented by Hsps from adjacent glial cells. Hence, application of  
 exogenous Hsps at neural injury sites is an effective strategy to maintain  
 neuronal viability.  
 L4 ANSWER 11 OF 28 BIOSIS COPYRIGHT (c) 2011 The Thomson Corporation on  
 STN  
 ACCESSION NUMBER: 2007:148222 BIOSIS  
 DOCUMENT NUMBER: PREV200700151256  
 TITLE: A multicenter, dose ranging safety and pharmacokinetics  
 study of arimoclomol in ALS.  
 AUTHOR(S): Cudkowicz, Merit E.; Shefner, Jeremy; Brown, Robert H.;  
 Simpson, Elizabeth; Yu, Hong; Zhang, Hui; Opoliner, April;  
 Taft, Jim; Grasso, Daniela; Schoenfeld, David; Wieland,  
 Scott; Barber, Jack; NEALS Arimoclomol Sites [Reprint  
 Author]  
 SOURCE: Annals of Neurology, (2006) Vol. 60, No. Suppl. 10, pp.  
 S13.  
 Meeting Info.: 131st Annual Meeting of the  
 American-Neurological-Association. Chicago, IL, USA.  
 October 08 -11, 2006. Amer Neurol Assoc.  
 CODEN: ANND3. ISSN: 0364-5134.  
 DOCUMENT TYPE: Conference; (Meeting)

Conference; Abstract; (Meeting Abstract)  
LANGUAGE: English  
ENTRY DATE: Entered STN: 7 Mar 2007  
Last Updated on STN: 7 Mar 2007

L4 ANSWER 12 OF 28 EMBASE COPYRIGHT (c) 2011 Elsevier B.V. All rights reserved on STN

ACCESSION NUMBER: 2010642838 EMBASE  
TITLE: Genetic determinants of amyotrophic lateral sclerosis as therapeutic targets.  
AUTHOR: Bosco, Daryl A.; Landers, John E.  
CORPORATE SOURCE: Department of Neurology, University of Massachusetts Medical School, Worcester, MA 01605, United States. john.landersonumassmed.edu; daryl.bosco@umassmed.edu  
AUTHOR: Bosco, D. A. (correspondence)  
CORPORATE SOURCE: Department of Neurology, University of Massachusetts Medical School, Worcester, MA 01605, United States. daryl.bosco@umassmed.edu  
SOURCE: CNS and Neurological Disorders - Drug Targets, (2010) Vol. 9, No. 6, pp. 779-790.  
Refs: 158  
ISSN: 1871-5273  
PUBLISHER: Bentham Science Publishers B.V., P.O. Box 294, Bussum, 1400 AG, Netherlands.  
COUNTRY: Netherlands  
DOCUMENT TYPE: Journal; Article  
FILE SEGMENT: 006 Internal Medicine  
008 Neurology and Neurosurgery  
022 Human Genetics  
030 Clinical and Experimental Pharmacology  
037 Drug Literature Index  
039 Pharmacy  
LANGUAGE: English  
SUMMARY LANGUAGE: English  
ENTRY DATE: Entered STN: 9 Dec 2010  
Last Updated on STN: 9 Dec 2010

AB Amyotrophic lateral sclerosis (ALS) is an incurable disease resulting from the deterioration of motor neurons. The onset of disease typically occurs in the fifth decade of life and progresses rapidly; death occurs for 75% of patients within 5 years. The only drug that is available to treat ALS is riluzole, which extends survival by just 2-3 months. Thus, new therapeutic directions are being sought to prolong the lifespan of ALS patients. Since the discovery of SOD1 as a genetic determinant of ALS in 1993, SOD1-models of ALS have been extensively employed for the development of ALS therapeutics. Novel genetic targets are now under investigation following the recent discoveries linking TDP-43, FUS/TLS, angiogenin, KIFAP3 and UNC13A to ALS. In this review, we present several of the genetic contributors to both sporadic and familial forms of ALS and discuss their potential as therapeutic targets for this devastating disease. .COPYRGHT. 2010 Bentham Science Publishers.

L4 ANSWER 13 OF 28 EMBASE COPYRIGHT (c) 2011 Elsevier B.V. All rights reserved on STN

ACCESSION NUMBER: 2010374588 EMBASE  
TITLE: Clinical trials for neuroprotection in ALS.  
AUTHOR: Siciliano, G. (correspondence); Carlesi, C.; Pasquali, L.; Piazza, S.; Murri, L.  
CORPORATE SOURCE: Department of Neuroscience, Clinical Neurology, University of Pisa, via Roma 67, 56126 Pisa, Italy. g.siciliano@med.unipi.it  
AUTHOR: Fornai, F.

CORPORATE SOURCE: Department of Human Morphology and Applied Biology,  
University of Pisa, Pisa, Italy.  
AUTHOR: Pietracupa, S.; Fornai, F.; Ruggieri, S.  
CORPORATE SOURCE: Laboratory of Neurobiology of Movement Disorders INM, IRCCS  
Neuromed, Pozzilli, Isernia, Italy.  
SOURCE: CNS and Neurological Disorders - Drug Targets, (2010) Vol.  
9, No. 3, pp. 305-313.  
Refs: 99  
ISSN: 1871-5273  
PUBLISHER: Bentham Science Publishers B.V., P.O. Box 294, Bussum, 1400  
AG, Netherlands.  
COUNTRY: Netherlands  
DOCUMENT TYPE: Journal; Article  
FILE SEGMENT: 005 General Pathology and Pathological Anatomy  
006 Internal Medicine  
008 Neurology and Neurosurgery  
037 Drug Literature Index  
038 Adverse Reactions Titles  
FILE SEGMENT: ClinicalTrials.gov  
CLINICAL TRIAL NO.: NCT00035815; NCT00047723; NCT00140450; NCT00231140;  
NCT00243932; NCT00349622; NCT00696332; NCT00706147;  
NCT00800501; NCT00818389; NCT00877604; NCT00982150  
LANGUAGE: English  
SUMMARY LANGUAGE: English  
ENTRY DATE: Entered STN: 22 Jul 2010  
Last Updated on STN: 22 Jul 2010

AB Owing to uncertainty on the pathogenic mechanisms underlying motor neuron  
degeneration in amyotrophic lateral sclerosis (ALS) riluzole  
remains the only available therapy, with only marginal effects on disease  
survival. Here we review some of the recent advances in the search for  
disease-modifying drugs for ALS based on their putative  
neuroprotective effects. A number of more or less established agents have  
recently been investigated also in ALS for their potential role  
in neuroprotection and relying on antilutamatergic, antioxidant or  
antiapoptotic strategies. Among them Talampanel, beta-lactam antibiotics,  
Coenzyme Q10, and minocycline have been investigated. Progress has also  
been made in exploiting growth factors for the treatment of ALS,  
partly due to advances in developing effective delivery systems to the  
central nervous system. A number of new therapies have also been  
identified, including a novel class of compounds, such as heat-shock  
protein co-inducers, which upregulate cell stress responses, and agents  
promoting autophagy and mitochondriogenesis, such as lithium and  
rapamycin. More recently, alterations of mRNA processing were described  
as a pathogenic mechanism in genetically defined forms of ALS,  
as those related to TDP-43 and FUS-TLS gene mutations. This knowledge is  
expected to improve our understanding of the pathogenetic mechanism in  
ALS and developing more effective therapies. .COPYRG. 2010  
Bentham Science Publishers Ltd.

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ACCESSION NUMBER: 2010169751 EMBASE  
TITLE: Motor neuron disease: Systematic reviews of treatment for  
ALS and SMA.  
AUTHOR: Orrell, Richard W.  
CORPORATE SOURCE: Department of Clinical Neuroscience, Institute of  
Neurology, University College London, Rowland Hill Street,  
London NW3 2QG, United Kingdom. r.orrell@ucl.ac.uk  
AUTHOR: Orrell, R. W., Dr. (correspondence)  
CORPORATE SOURCE: Department of Clinical Neuroscience, Institute of  
Neurology, University College London, Rowland Hill Street,  
London NW3 2QG, United Kingdom. r.orrell@ucl.ac.uk

SOURCE: British Medical Bulletin, (March 2010) Vol. 93, No. 1, pp. 145-159.  
 Refs: 51  
 ISSN: 0007-1420; E-ISSN: 1471-8391 CODEN: BMBUAQ  
 PUBLISHER: Oxford University Press, Great Clarendon Street, Oxford, OX2 6DP, United Kingdom.  
 COUNTRY: United Kingdom  
 DOCUMENT TYPE: Journal; General Review; (Review)  
 FILE SEGMENT: 008 Neurology and Neurosurgery  
 036 Health Policy, Economics and Management  
 037 Drug Literature Index  
 038 Adverse Reactions Titles  
 039 Pharmacy  
 LANGUAGE: English  
 SUMMARY LANGUAGE: English  
 ENTRY DATE: Entered STN: 19 Apr 2010  
 Last Updated on STN: 19 Apr 2010

AB Introduction: There is no curative treatment for the common motor neuron diseases, amyotrophic lateral sclerosis (ALS) and spinal muscular atrophy. Nevertheless, there is an increasing volume of published studies. This review assesses the current evidence for treatment of these conditions. Sources of data: Primarily, the systematic reviews of the Cochrane Collaboration, with additional reference to other systematic reviews and online sites. Areas of agreement: Riluzole remains the only medication with demonstrated efficacy and regulatory approval for the treatment of ALS. Areas of controversy, growing points and areas timely for developing research: The design of clinical trials and the publication of unsatisfactory studies, in both human and animal models, continue to cause confusion in advising on patient management. Improvements in trial design, critical assessment of studies for publication and avoidance of bias towards publication of positive results are needed. A better understanding of pathogenesis should lead to more potent interventions. .COPYRG. The Author 2009. Published by Oxford University Press. All rights reserved.

L4 ANSWER 15 OF 28 EMBASE COPYRIGHT (c) 2011 Elsevier B.V. All rights reserved on STN

ACCESSION NUMBER: 2009405567 EMBASE  
 TITLE: [Update on fundamental and clinical research in amyotrophic lateral sclerosis].  
 Actualites dans la recherche fondamentale et clinique sur la sclerose laterale amyotrophique.  
 AUTHOR: Pradat, P.-F. (correspondence); Gonzalez, J.  
 CORPORATE SOURCE: Centre SLA de Paris, Federation des Maladies du Systeme Nerveux, AP-HP, 47, boulevard de l'Hopital, 75651 Paris cedex 13, France. pierre-francois.pradat@psl.ap-hop-paris.fr  
 AUTHOR: Camdessanche, J.-P.  
 CORPORATE SOURCE: Centre SLA de Saint-Etienne, Hopital Bellevue, Saint-Etienne, France.  
 AUTHOR: Carlier, L.  
 CORPORATE SOURCE: Centre SLA de Caen, Hopital Cote-de-Nacre, Caen, France.  
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 CORPORATE SOURCE: Centre SLA de Toulouse, Hopital de Rangueil, Toulouse, France.  
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 CORPORATE SOURCE: Centre SLA de Tours, Hopital Bretonneau, Tours, France.  
 AUTHOR: Danel-Brunaud, V.  
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 AUTHOR: Echaniz-Laguna, A.  
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 .

AUTHOR: Nicolas, G.  
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 .  
 AUTHOR: Verschuere, A.  
 CORPORATE SOURCE: Centre SLA de Marseille, Hopital de la Timone, Marseille, France.  
 SOURCE: Revue Neurologique, (June/July 2009) Vol. 165, No. 6-7, pp. 532-541.  
 Refs: 53  
 ISSN: 0035-3787 CODEN: RENEAM  
 PUBLISHER: Elsevier Masson SAS, 62 rue Camille Desmoulins, Issy les Moulineaux Cedex, 92442, France.  
 PUBLISHER IDENT.: S 0035-3787(09)00078-2  
 COUNTRY: France  
 DOCUMENT TYPE: Journal; General Review; (Review)  
 FILE SEGMENT: 005 General Pathology and Pathological Anatomy  
 008 Neurology and Neurosurgery  
 017 Public Health, Social Medicine and Epidemiology  
 037 Drug Literature Index  
 LANGUAGE: French  
 SUMMARY LANGUAGE: English; French  
 ENTRY DATE: Entered STN: 7 Sep 2009  
 Last Updated on STN: 7 Sep 2009  
 AB This paper from a group of French experts in amyotrophic lateral sclerosis (ALS) presents an update of recent advances in fundamental, epidemiological and clinical research in ALS. Recent development in the pathogenesis of ALS suggests that motor neuron degeneration is a multifactorial and noncell autonomous process. Research has been advanced through the identification of the TAR-DNA-binding protein (TDP-43) as a common neuropathological marker of ALS and frontotemporal lobar degeneration with ubiquitin-positive inclusions. Recently, mutations in the TDP-43 gene have been described in individuals with familial and sporadic ALS. Fundamental research in ALS is expected to lead to the disclosure of new diagnostic markers and therapeutic targets. A small trial has suggested that lithium carbonate may slow ALS progression but larger trials will be needed to confirm these results. .COPYRG. 2009 Elsevier Masson SAS.  
 L4 ANSWER 16 OF 28 EMBASE COPYRIGHT (c) 2011 Elsevier B.V. All rights reserved on STN  
 ACCESSION NUMBER: 2009095161 EMBASE  
 TITLE: Managing amyotrophic lateral sclerosis: Slowing disease progression and improving patient quality of life.  
 AUTHOR: Brooks, Benjamin Rix  
 CORPORATE SOURCE: University of Wisconsin, School of Medicine and Public Health, Madison, WI. benjamin.brooks@carolinashealthcare.org  
 AUTHOR: Brooks, Benjamin Rix  
 CORPORATE SOURCE: Carolinas Neuromuscular/Amyotrophic Lateral Sclerosis, Muscular Dystrophy Association Center, Charlotte, NC. benjamin.brooks@carolinashealthcare.org  
 AUTHOR: Brooks, Benjamin Rix  
 CORPORATE SOURCE: Carolinas Neuromuscular/ALS-MDA Center, Neuroscience and Spine Institute, Carolinas Medical Center, 1010 Edgehill Road North, Charlotte, NC 28207-1885. benjamin.brooks@carolinashealthcare.org  
 AUTHOR: Brooks, B. R., Dr. (correspondence)  
 CORPORATE SOURCE: Carolinas Neuromuscular/ALS-MDA Center, Neuroscience and Spine Institute, Carolinas Medical Center, 1010 Edgehill

Road North, Charlotte, NC 28207-1885. benjamin.brooks@carolinashealthcare.org  
 Annals of Neurology, (January 2009) Vol. 65, No. SUPPL. 1, pp. S17-S23.  
 Refs: 85  
 ISSN: 0364-5134; E-ISSN: 1531-8249 CODEN: ANNE3D  
 PUBLISHER: John Wiley and Sons Inc., P.O.Box 18667, Newark, NJ 07191-8667, United States.  
 COUNTRY: United States  
 DOCUMENT TYPE: Journal; General Review; (Review)  
 FILE SEGMENT: 005 General Pathology and Pathological Anatomy  
 006 Internal Medicine  
 008 Neurology and Neurosurgery  
 037 Drug Literature Index  
 038 Adverse Reactions Titles  
 LANGUAGE: English  
 SUMMARY LANGUAGE: English  
 ENTRY DATE: Entered STN: 10 Mar 2009  
 Last Updated on STN: 10 Mar 2009

AB It is now possible to slow the disease progression of amyotrophic lateral sclerosis (ALS), but documented improvement in the quality of life of ALS patients has been difficult to quantitate. Putative mechanisms involved in motor neuron degeneration in ALS include oxidative damage, mitochondrial dysfunction, neuroinflammation, growth factor deficiency, and glutamate excitotoxicity. Several pharmacological agents that target these potential targets have demonstrated therapeutic potential in animal models with mutations in the gene encoding Cu/Zn superoxide dismutase (SOD1). Many treatments that have been moderately effective in this animal model have not been successfully translated into effective treatments for humans with ALS. Only the glutamate modulator riluzole has demonstrated efficacy in clinical trials and is approved for treating ALS. Combination treatments may represent a potential therapeutic strategy to more robustly prolong life and preserve function, but only vitamin E with riluzole has been formally studied in clinical trials, and to date, no combination treatments have been found to be more effective than currently available single agents.  
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ACCESSION NUMBER: 2008532366 EMBASE  
 TITLE: [Minocycline for the treatment of amyotrophic lateral sclerosis: Neuroprotector or neurotoxin? Reflections on another failure of translational medicine].  
 Minociclina para el tratamiento de la esclerosis lateral amiotrofica: Neuroprotectora o neurotoxica? Reflexiones sobre otro fracaso de la medicina traslacional.  
 AUTHOR: Gamez, Josep (correspondence)  
 CORPORATE SOURCE: Clinica de Enfermedades Neuromusculares, Departamento de Neurologia, Universidad Autonoma de Barcelona (UAB), Passeig Vall d'Hebron, 119, Barcelona, Spain. 12784jgc@comb.es

SOURCE: Neurologia, (October 2008) Vol. 23, No. 8, pp. 484-493.  
 Refs: 170  
 ISSN: 0213-4853; E-ISSN: 1578-1968 CODEN: NERLEN  
 PUBLISHER: STM Editores S.A, Principe de Vergara 211, Esc Izda 60D, Madrid, 28002, Spain.  
 COUNTRY: Spain  
 DOCUMENT TYPE: Journal; General Review; (Review)  
 FILE SEGMENT: 008 Neurology and Neurosurgery  
 037 Drug Literature Index

038 Adverse Reactions Titles  
LANGUAGE: Spanish; Castilian  
SUMMARY LANGUAGE: English; Spanish; Castilian  
ENTRY DATE: Entered STN: 3 Dec 2008  
Last Updated on STN: 3 Dec 2008

AB A recent publication of the results of a clinical trial of minocycline in 412 ALS patient has aroused considerable controversy in the ALS scientific community. As on previous occasions, the results obtained in the laboratory are not reproduced in clinical practice. The reasons for this new disappointment in translational medicine are analysed by applying the successes obtained in the experimental animal model for ALS to humans. The most frequently suggested causes for explaining these continuous failures are unawareness of the correct dosage to be used, the ideal duration of the clinical trial in phase III, sample size, the search for a primary outcome for measurement other than survival, the need for biomarkers giving information on the progression of the disease and whether this is modified by the introduction of the drug for study. Debate focuses on whether the transgenic mouse model of ALS which expresses SOD 1 mutations which we have been using for more than a decade is an exact reflection of the clinical profile and the pathophysiologic mechanisms present in patients with sporadic ALS. There is the possibility that depending on the dose administered, minocycline can be a neuroprotector or a neurotoxin. In other words, at a dose of 200 mg/day, this drug behaves like «Dr. Jekyll» and like «Mr. Hyde» at doses of 400 mg. For the authors of the trial, this possibility does not seem to be the cause of the disappointing results obtained. However, they acknowledge that one of the limitations of their study was that it was impossible to compare the effects of minocycline in the patient after receiving 200 or 400 mg. For many other researchers running ongoing clinical trials in both ALS and other neurological diseases, the dose of 200 mg/day is chosen as ideal for testing the effectiveness of minocycline in patients. The strategy of administering the maximum dose of a drug to be tested may give rise to misleading results. We agree with the opinion of other authors, who say that minocycline should be given a second chance.

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ACCESSION NUMBER: 2008461689 EMBASE  
TITLE: ALS Drug Development: Reflections from the Past and a Way Forward.  
AUTHOR: Aggarwal, Swati (correspondence); Cudkowicz, Merit  
CORPORATE SOURCE: Department of Neurology, Massachusetts General Hospital, Neurology Clinical Trials Unit, Charlestown, MA 02129, United States. spaggarwal@partners.org  
SOURCE: Neurotherapeutics, (October 2008) Vol. 5, No. 4, pp. 516-527.  
Refs: 69  
ISSN: 1933-7213  
PUBLISHER: Elsevier Inc., 360 Park Avenue South, New York, NY 10010, United States.  
PUBLISHER IDENT.: S 1933-7213(08)00141-4  
COUNTRY: United States  
DOCUMENT TYPE: Journal; Article  
FILE SEGMENT: 008 Neurology and Neurosurgery  
022 Human Genetics  
037 Drug Literature Index  
038 Adverse Reactions Titles  
LANGUAGE: English  
SUMMARY LANGUAGE: English  
ENTRY DATE: Entered STN: 10 Nov 2008  
Last Updated on STN: 10 Nov 2008

AB Tremendous advances in our understanding of pathogenesis of amyotrophic lateral sclerosis (ALS) have provided a rich pipeline of drugs for clinical trials. At least 32 unique compounds have been tested. Nevertheless, riluzole is currently the only treatment that prolongs survival. We present a critical overview of past clinical trials, how therapies are selected for testing in people, challenges with ALS clinical trial design and conduct, and ways to best move forward.  
.COPYRG. 2008.

L4 ANSWER 19 OF 28 EMBASE COPYRIGHT (c) 2011 Elsevier B.V. All rights reserved on STN

ACCESSION NUMBER: 2008453896 EMBASE  
TITLE: Scrutinizing enrollment in ALS clinical trials:  
Room for improvement?  
AUTHOR: Bedlack, Richard S. (correspondence); Pastula, Daniel  
CORPORATE SOURCE: Duke University Medical Center, Durham, NC, United States.  
AUTHOR: Welsh, Emily; Pulley, Darlene; Cudkowicz, Merit E.  
CORPORATE SOURCE: Neurology Clinical Trial Unit, Massachusetts General Hospital, Charlestown, MA, United States.  
SOURCE: Amyotrophic Lateral Sclerosis, (2008) Vol. 9, No. 5, pp. 257-265.  
Refs: 27  
ISSN: 1748-2968; E-ISSN: 1471-180X  
PUBLISHER: Taylor and Francis Ltd., 4 Park Square, Milton Park, Abingdon, Oxfordshire, OX14 4RN, United Kingdom.  
PUBLISHER IDENT.: 794219329  
COUNTRY: United Kingdom  
DOCUMENT TYPE: Journal; Article  
FILE SEGMENT: 008 Neurology and Neurosurgery  
017 Public Health, Social Medicine and Epidemiology  
037 Drug Literature Index  
LANGUAGE: English  
SUMMARY LANGUAGE: English  
ENTRY DATE: Entered STN: 16 Oct 2008  
Last Updated on STN: 16 Oct 2008

AB Enrollment in ALS trials has not been systematically studied. We surveyed the ALS Research Group (ALSRG) to learn their impressions of enrollment at ALS clinics across North America. We also reviewed completed ALS trials to determine an enrollment rate (subjects per site per month), its variability across trials, whether it is changing over time, and whether it is influenced by 'trial factors'. ALSRG members were polled via an online survey. ALS trials were identified by literature review and investigator contact. Enrollment rate versus publication year was plotted for each trial. Models were created to examine how 'trial factors' were associated with enrollment rate. By survey, percent enrollment is 25% and highly variable (range 0-75%). By literature review, enrollment rate is 2.2 participants/site/month and highly variable (range 0.1-7.5). Enrollment is not improving over time; no 'trial factor' explains the variability in enrollment across trials. Behaviors among clinic directors and patients were identified that may influence enrollment. In conclusion, ALS trial enrollment rate is low, highly variable and not influenced by trial design factors. 'Patient factors' and 'physician factors' may play more important roles in influencing enrollment, as in oncology trials. Our survey data support this idea, and provide potential mechanisms for improving enrollment.

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ACCESSION NUMBER: 2008336544 EMBASE  
TITLE: Therapy development for ALS: Lessons learned and path forward.  
AUTHOR: Lanka, Veena; Cudkowicz, Merit (correspondence)



CORPORATE SOURCE: Neurology Clinical Trials Unit, Massachusetts General Hospital, Harvard Medical School, Charlestown, MA, United States.

SOURCE: Amyotrophic Lateral Sclerosis, (2008) Vol. 9, No. 3, pp. 131-140.  
Refs: 112  
ISSN: 1748-2968; E-ISSN: 1471-180X

PUBLISHER: Taylor and Francis Ltd., 4 Park Square, Milton Park, Abingdon, Oxfordshire, OX14 4RN, United Kingdom.

PUBLISHER IDENT.: 7931503/5

COUNTRY: United Kingdom

DOCUMENT TYPE: Journal; General Review; (Review)

FILE SEGMENT: 005 General Pathology and Pathological Anatomy  
008 Neurology and Neurosurgery  
029 Clinical and Experimental Biochemistry  
030 Clinical and Experimental Pharmacology  
037 Drug Literature Index  
038 Adverse Reactions Titles

LANGUAGE: English

SUMMARY LANGUAGE: English

ENTRY DATE: Entered STN: 24 Jul 2008  
Last Updated on STN: 24 Jul 2008

AB Several therapies have shown promise in preclinical models of motor neuron disease. Several of these treatment approaches, however, failed in human studies. In moving forward with new promising therapies, it is important to first identify whether the past trials were unsuccessful due to wrong therapy and biological target or because of flaws in trial design and conduct. We review treatment development in ALS and discuss the strengths and limitations of past clinical trials. Better biomarkers of disease and markers of biological activity of the therapies under development are urgently needed. Obtaining information regarding dosage, pharmacokinetics, short-term safety and biological activity in well designed phase I and II studies is critical to the design of phase III trials that will yield meaningful results.

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ACCESSION NUMBER: 2008326797 EMBASE

TITLE: Drug Therapy in Amyotrophic Lateral Sclerosis.

AUTHOR: Distad, B. Jane, Dr. (correspondence); Meekins, Gregg D.; Liou, Lee L.; Weiss, Michael D.

CORPORATE SOURCE: Department of Neurology, University of Washington Medical Center, 1959 NE Pacific Street, Seattle, WA 98195, United States. jdistad@u.washington.edu

AUTHOR: Carter, Gregory T.

CORPORATE SOURCE: Department of Physical Medicine and Rehabilitation, University of Washington Medical Center, 1959 NE Pacific Street, Seattle, WA 98195, United States.

AUTHOR: Miller, Robert G.

CORPORATE SOURCE: California Pacific Medical Center, Forbes Norris MDA/ALS Research Center, 2324 Sacramento Street #111, San Francisco, CA 94115, United States.

SOURCE: Physical Medicine and Rehabilitation Clinics of North America, (August 2008) Vol. 19, No. 3, pp. 633-651.  
Refs: 154  
ISSN: 1047-9651 CODEN: PMRAFZ

PUBLISHER: W.B. Saunders, Independence Square West, Philadelphia, PA 19106-3399, United States.

PUBLISHER IDENT.: S 1047-9651(08)00033-8

COUNTRY: United States

DOCUMENT TYPE: Journal; General Review; (Review)

FILE SEGMENT: 006 Internal Medicine

008 Neurology and Neurosurgery  
 019 Rehabilitation and Physical Medicine  
 030 Clinical and Experimental Pharmacology  
 037 Drug Literature Index  
 038 Adverse Reactions Titles

FILE SEGMENT: ClinicalTrials.gov

CLINICAL TRIAL NO.: NCT00353665; NCT00403104; NCT00409721

LANGUAGE: English

SUMMARY LANGUAGE: English

ENTRY DATE: Entered STN: 20 Aug 2008

Last Updated on STN: 20 Aug 2008

AB Amyotrophic lateral sclerosis (ALS) is a devastating condition characterized by progressive muscle wasting, inanition, respiratory failure, and death within approximately 2 to 5 years of onset. ALS is among the most common neuromuscular conditions, with an overall prevalence in the world of 5 to 7 cases/100,000 population. Epidemiologic studies have identified some potential risk factors for developing ALS, including a high-fat, low-fiber diet; cigarette smoking; slimness and athleticism; and living in urban areas. Between 5% and 10% of ALS is genetic, with up to 11 genetic loci identified. Although understanding of the pathophysiology of this disease has advanced over the past 60 years, scant progress has been made regarding effective treatment. The authors review the current understanding of the pathogenic mechanisms of ALS and approaches to treating the disease. .COPYRGT. 2008 Elsevier Inc. All rights reserved.

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ACCESSION NUMBER: 2008288080 EMBASE

TITLE: A recipe for ALS.

AUTHOR: Shoesmith, Christen (correspondence)

AUTHOR: Shoesmith, Christen (correspondence)

CORPORATE SOURCE: London, ON, Canada.

SOURCE: Canadian Journal of Neurological Sciences, (May 2008) Vol. 35, No. 2, pp. 125-126.

Refs: 13

ISSN: 0317-1671 CODEN: CJNSA2

PUBLISHER: Canadian Journal of Neurological Sciences, P.O. Box 5456, Station A, Calgary, AB T2H 1X8, Canada.

COUNTRY: Canada

DOCUMENT TYPE: Journal, Editorial

FILE SEGMENT: 008 Neurology and Neurosurgery  
 017 Public Health, Social Medicine and Epidemiology  
 026 Immunology, Serology and Transplantation  
 029 Clinical and Experimental Biochemistry  
 037 Drug Literature Index

LANGUAGE: English

ENTRY DATE: Entered STN: 22 Jul 2008

Last Updated on STN: 22 Jul 2008

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ACCESSION NUMBER: 2008277583 EMBASE

TITLE: [Amyotrophic lateral sclerosis. Current clinical trials and underlying pathomechanisms].

Amyotrophe lateralsklerose. Aktuelle klinische studien und ihr pathogenetischer hintergrund.

AUTHOR: Kollwe, K., Dr. (correspondence); Dengler, R.; Petri, S.

CORPORATE SOURCE: Neurologische Klinik Mit Klinischer Neurophysiologie, Medizinische Hochschule Hannover, Carl-Neuberg-Strasse 1, 30625 Hannover, Germany. Kollwe.Katja@mh-hannover.de

SOURCE: Nervenarzt, (Jun 2008) Vol. 79, No. 6, pp. 653-661.  
 Refs: 81  
 ISSN: 0028-2804 CODEN: NERVAF  
 COUNTRY: Germany  
 DOCUMENT TYPE: Journal; General Review; (Review)  
 FILE SEGMENT: 017 Public Health, Social Medicine and Epidemiology  
 037 Drug Literature Index  
 008 Neurology and Neurosurgery  
 LANGUAGE: German  
 SUMMARY LANGUAGE: English; German  
 ENTRY DATE: Entered STN: 15 Jul 2008  
 Last Updated on STN: 15 Jul 2008

AB Amyotrophic lateral sclerosis (ALS) is a neurodegenerative disease leading to death after 3 to 5 years. The glutamate antagonist Riluzole currently is the only drug with marginal therapeutic benefit, but its effect on survival is modest, with an average increase of only 3-4 months. Therefore symptomatic treatment still is the most important. Further neuroprotective agents are currently under investigation, both in transgenic animal models of ALS and clinical trials in ALS patients. This review summarizes the current state of clinical studies in ALS patients in the context of underlying therapeutic mechanisms. .COPYRG. 2008 Springer Medizin Verlag.

L4 ANSWER 24 OF 28 EMBASE COPYRIGHT (c) 2011 Elsevier B.V. All rights reserved on STN

ACCESSION NUMBER: 2006564553 EMBASE  
 TITLE: Translating preclinical insights into effective human trials in ALS.  
 AUTHOR: DiBernardo, Allitia B. (correspondence); Cudkowicz, Merit E.  
 CORPORATE SOURCE: Department of Neurology, Massachusetts General Hospital, Boston, MA 02129, United States. adibernardo@partners.org  
 SOURCE: Biochimica et Biophysica Acta - Molecular Basis of Disease, (Nov 2006) Vol. 1762, No. 11-12, pp. 1139-1149.  
 Refs: 132  
 ISSN: 0925-4439 CODEN: BBADEX  
 S 0925-4439(06)00051-2  
 PUBLISHER IDENT.: Netherlands  
 COUNTRY: Netherlands  
 DOCUMENT TYPE: Journal; General Review; (Review)  
 FILE SEGMENT: 037 Drug Literature Index  
 008 Neurology and Neurosurgery  
 LANGUAGE: English  
 SUMMARY LANGUAGE: English  
 ENTRY DATE: Entered STN: 2 Jan 2007  
 Last Updated on STN: 2 Jan 2007

AB Amyotrophic lateral sclerosis (ALS) is a rapidly progressive, adult-onset neurodegenerative disease characterized by selective dysfunction and death of motor neurons in the brain and spinal cord. The disease is typically fatal within 3-5 years of symptom onset. There is no known cure and only riluzole, which was approved by the FDA in 1996 for treatment of ALS, has shown some efficacy in humans. Preclinical insights from model systems continue to furnish ample therapeutic targets, however, translation into effective therapies for humans remains challenging. We present an overview of clinical trial methodology for ALS, including a summary rationale for target selection and challenges to ALS clinical research. .COPYRG. 2006 Elsevier B.V. All rights reserved.

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ACCESSION NUMBER: 2006561568 EMBASE  
 TITLE: Failure of protein quality control in amyotrophic lateral

sclerosis.

AUTHOR: Kabashi, Edor; Durham, Heather D. (correspondence)  
 CORPORATE SOURCE: Department of Neurology, Neurosurgery and Montreal  
 Neurological Institute, McGill University, 3801 University  
 St, Montreal, Que. H3A 2B4, Canada. heather.durham@mcgill.ca

SOURCE: Biochimica et Biophysica Acta - Molecular Basis of Disease,  
 (Nov 2006) Vol. 1762, No. 11-12, pp. 1038-1050.  
 Refs: 151  
 ISSN: 0925-4439 CODEN: BBADEX  
 S 0925-4439(06)00114-1

PUBLISHER IDENT.: S 0925-4439(06)00114-1  
 COUNTRY: Netherlands

DOCUMENT TYPE: Journal; General Review; (Review)  
 FILE SEGMENT: 030 Clinical and Experimental Pharmacology  
 037 Drug Literature Index  
 038 Adverse Reactions Titles  
 005 General Pathology and Pathological Anatomy  
 008 Neurology and Neurosurgery

LANGUAGE: English  
 SUMMARY LANGUAGE: English  
 ENTRY DATE: Entered STN: 28 Dec 2006  
 Last Updated on STN: 28 Dec 2006

AB The protein chaperoning and ubiquitin-proteasome systems perform many  
 homeostatic functions within cells involving protein folding, transport  
 and degradation. Of paramount importance is ridding cells of mutant or  
 post-translationally modified proteins that otherwise tend to aggregate  
 into insoluble complexes and form inclusions. Such inclusions are  
 characteristic of many neurodegenerative diseases and implicate protein  
 misfolding and aggregation as common aspects of pathogenesis. In the most  
 common familial form of ALS, mutations in SOD1 promote  
 misfolding of the protein and target it for degradation by proteasomes.  
 Although proteasomes can degrade the mutant proteins efficiently, altered  
 solubility and aggregation of mutant SOD1 are features of the disease and  
 occur most prominently in the most vulnerable cells and tissues. Indeed,  
 lumbar spinal cord of mutant SOD1 transgenic mice show early reduction in  
 their capacity for protein chaperoning and proteasome-mediated hydrolysis  
 of substrates, and motor neurons are particularly vulnerable to  
 aggregation of mutant SOD1. A high threshold for upregulating key  
 pathways in response to the stress of added substrate load may contribute  
 to this vulnerability. The broad spectrum neuroprotective capability and  
 efficacy of some chaperone-based therapies in preclinical models makes  
 these pathways attractive as targets for therapy in ALS, as well  
 as other neurodegenerative diseases. A better understanding of the  
 mechanisms governing the regulation of protein chaperones and UPS  
 components would facilitate development of treatments that upregulate  
 these pathways in a coordinated manner in neural tissue without long term  
 toxicity. .COPYRG. 2006 Elsevier B.V. All rights reserved.

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ACCESSION NUMBER: 2006561567 EMBASE

TITLE: Gene Therapy for ALS: Progress and prospects.  
 AUTHOR: Azzouz, Mimoun (correspondence)  
 CORPORATE SOURCE: Academic Unit of Neurology, Medical School, The University  
 of Sheffield, Beech Hill Road, Sheffield, S10 2RX, United  
 Kingdom. m.azzouz@sheffield.ac.uk

SOURCE: Biochimica et Biophysica Acta - Molecular Basis of Disease,  
 (Nov 2006) Vol. 1762, No. 11-12, pp. 1122-1127.  
 Refs: 85  
 ISSN: 0925-4439 CODEN: BBADEX  
 S 0925-4439(06)00083-4

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AB Amyotrophic lateral sclerosis (ALS) is a devastating disease for which there are no effective drug treatments to date. Recent advances in Gene Therapy open up the possibility of developing an effective treatment aiming at halting or delaying the degeneration of motor neurons. Viral vectors such as lentiviral vectors and adeno-associated virus can transfer genes into many different types of primary neurons from a broad range of species including man and the resulting gene expression is long-term. Numerous animal studies have now been undertaken with these vectors and correction of disease models has been obtained. These vectors have been refined to a very high level and can be produced safely for the clinic. However, we believe that there are some major issues that need to be addressed in order to see a Gene Therapy approach with viral vectors proceed to the clinic for ALS patients. This review will describe the general features of lentiviral vectors. It will then describe some key examples of gene transfer and genetic correction in animal models of motor neuron disease. The prospects for the clinical evaluation of lentiviral vectors for the treatment of human motor neuron disease will be outlined. .COPYRG. 2006 Elsevier B.V. All rights reserved.

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ACCESSION NUMBER: 2006209819 EMBASE

TITLE: Targets in ALS: designing multidrug therapies.

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SOURCE: Trends in Pharmacological Sciences, (May 2006) Vol. 27, No. 5, pp. 267-273.

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AB Amyotrophic lateral sclerosis (ALS) is an incurable disease that arises from the progressive loss of motoneurons. Even when caused by a single gene defect, as in the case of mutations in the enzyme Cu-Zn

superoxide dismutase (SOD1), ALS is the result of a complex cascade that involves crosstalk among motoneurons, glia and muscles, and evolves through the action of converging toxic mechanisms. Transgenic rodents that express human mutant SOD1 and develop a progressive paralytic disease are widely used to screen potential therapeutics. Treatments that interfere with a specific event in the neurotoxic cascade have been reported to produce a modest increase in rodent lifespan. Multi-intervention approaches, including novel methods to intercept the damage and to deliver molecules to vulnerable cells, have recently been shown to be more effective. Thus, new avenues for promising therapeutic approaches can be derived from multidrug treatments and/or the delivery of growth factors by viral vectors, in combination with exercise and/or diet regimens. .COPYRG. 2006 Elsevier Ltd. All rights reserved.

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ACCESSION NUMBER: 2006181530 EMBASE

TITLE: Therapeutic targets for amyotrophic lateral sclerosis: Current treatments and prospects for more effective therapies.

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SOURCE: Expert Review of Neurotherapeutics, (Mar 2006) Vol. 6, No. 3, pp. 417-428.

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AB Although amyotrophic lateral sclerosis (ALS) was described more than 130 years ago, the cause(s) of most cases of this adult motor neuron disease remains a mystery. With the discovery of mutations in one gene (Cu/Zn superoxide dismutase) as a primary cause of some forms of ALS, model systems have been developed that have helped us begin to understand mechanisms involved in motor neuron death and enabled testing of potential new therapies. Several other genes have been implicated as risk factors in motor neuron diseases, including neurofilaments, cytoplasmic dynein and dynactin, vascular endothelial growth factor, and angiogenin. With advances in the basic research of the disease, many hypotheses accounting for motor neuron death are being explored, including loss of trophic support, protein mishandling, mitochondrial dysfunction, excitotoxicity, axonal abnormalities and inflammation. Many of these mechanisms are the focus of research in other neurodegenerative disorders, such as Parkinson's, Alzheimer's and Huntington's disease. .COPYRG. 2006 Future Drugs Ltd.

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